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S ORF2 (S) (CLAVULANIC)
            2958  ORF2
           21765  CLAVULANIC
      S1       0  ORF2 (S) (CLAVULANIC)
?
S ORF2 (S) (STREPTOMYCES)
            2958  ORF2
           48674  STREPTOMYCES
      S2     214  ORF2 (S) (STREPTOMYCES)
?
S S2 AND (CLAVULANIC (W) ACID)
             214  S2
           21765  CLAVULANIC
         3710562  ACID
           21309  CLAVULANIC(W)ACID
      S3       0  S2 AND (CLAVULANIC (W) ACID)
?
S (CLAVULANIC) (S) (STREPTOMYCES)
           21765  CLAVULANIC
           48674  STREPTOMYCES
      S4     274  (CLAVULANIC) (S) (STREPTOMYCES)
?
S S4 AND ORF2
             274  S4
            2958  ORF2
      S5       0  S4 AND ORF2
?

Set     Items   Description
S1          0   ORF2 (S) (CLAVULANIC)
S2        214   ORF2 (S) (STREPTOMYCES)
S3          0   S2 AND (CLAVULANIC (W) ACID)
S4        274   (CLAVULANIC) (S) (STREPTOMYCES)
S5          0   S4 AND ORF2
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S S2 AND S4
             214  S2
             274  S4
      S6       0  S2 AND S4
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Set     Items   Description
S1          0   ORF2 (S) (CLAVULANIC)
S2        214   ORF2 (S) (STREPTOMYCES)
S3          0   S2 AND (CLAVULANIC (W) ACID)
S4        274   (CLAVULANIC) (S) (STREPTOMYCES)
S5          0   S4 AND ORF2
S6          0   S2 AND S4
?
S S2 AND (GENE (W) (CLUSTER OR CLONING))
             214  S2
         2342355  GENE
          139851  CLUSTER
          327717  CLONING
           30138  GENE(W)(CLUSTER OR CLONING)
      S7      81  S2 AND (GENE (W) (CLUSTER OR CLONING))
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...examined 50 records  (50)
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      S8      35  RD (unique items)
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             35  S8
        7269252  PY>1999
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S9 25 S8 NOT PY>1999
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T S9/3,K/ALL

9/3,K/1 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

14314584 PMID: 10220165
The tylosin biosynthetic cluster from Streptomyces fradiae: genetic organization of the left region.
Fouces R; Mellado E; Diez B; Barredo J L
Laboratorio de Ingenieria Genetica, Antibioticos SA, Leon, Spain.
Microbiology (Reading, England) (ENGLAND) Apr 1999, 145 (Pt 4) p855-68, ISSN 1350-0872 Journal Code: 9430468
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

The genetic organization of the left edge (tyIEDHFJ region) of the tylosin biosynthetic **gene cluster** from **Streptomyces** fradiae has been determined. Sequence analysis of a 12.9 kb region has revealed the presence of 11 ORFs, 10 of them belonging to the biosynthetic cluster. The putative functions of the proteins encoded by these genes are as follows: peptidase (ORF1, ddcA), tylosin resistance determinant (**ORF2** , tlrB), glycosyltransferase (ORF3, tylN), methyltransferase (ORF4, tylE), ketoreductase (ORF5, tylD), ferredoxin (ORF6, tylH2), cytochrome P450 (ORF7, tylH1), methyltransferase (ORF8, tylF), epimerase (ORF9, tylJ), acyl-CoA...

... tylosin idiotrophic mutants blocked at various stages in tylosin biosynthesis. The tlrB gene has been shown to be useful as a tylosin resistance marker in **Streptomyces** lividans, **Streptomyces** parvulus and **Streptomyces** coelicolor and the effect of tylF on macrocin depletion has been confirmed. A pathway for the biosynthesis of 6-deoxy-D-allose, the unmethylated mycinose...

9/3,K/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

14256152 PMID: 10077450
Nucleotide sequence of the gene cluster **containing the mphB gene for macrolide 2'-phosphotransferase II.**
Katayama J; Noguchi N
Department of Microbiology, School of Pharmacy, Tokyo University of Pharmacy and Life Science, Hachioji, Japan.
Biological & pharmaceutical bulletin (JAPAN) Feb 1999, 22 (2) p227-8 , ISSN 0918-6158 Journal Code: 9311984
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Nucleotide sequence of the gene cluster **containing the mphB gene for macrolide 2'-phosphotransferase II.**
... The DNA region of 6.5-kb EcoRI-PstI fragment contained five open reading frames (ORFs). ORF4 corresponded to mphB. Respective products deduced from ORF1, **ORF2** , ORF3, and ORF5 were similar to the penicillin-binding protein 4 of **Streptomyces** lactamduras, the repressor protein AcrR of the acrAB operon, the enzyme RdmC involved in the biosynthesis of the antibiotic aklavinone, and IS801 transposase-like protein from Pseudomonas pseudoalcakigenes, respectively. Among these

genes, **ORF2** , ORF3, and mphB formed a **gene cluster** with□ORF2□in the lead sequence. Our results suggest that mphB may originate from an operon related to antibiotic biosynthesis.

9/3,K/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

13639472 PMID: 9335272
Cloning of an avilamycin biosynthetic gene cluster **from Streptomyces viridochromogenes Tu57.**
Gaisser S; Trefzer A; Stockert S; Kirschning A; Bechthold A
Pharmazeutisches Institut, Pharmazeutische Biologie, Universitat Tubingen, Germany.
Journal of bacteriology (UNITED STATES) Oct 1997, 179 (20) p6271-8, ISSN 0021-9193 Journal Code: 2985120R
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Cloning of an avilamycin biosynthetic gene cluster **from Streptomyces viridochromogenes Tu57.**
A 65-kb region of DNA from **Streptomyces** viridochromogenes Tu57, containing genes encoding proteins involved in the biosynthesis of avilamycins, was isolated. The DNA sequence of a 6.4-kb fragment from this ...

... open reading frames (ORF1 to ORF4), three of which are fully contained within the sequenced fragment. The deduced amino acid sequence of AviM, encoded by **ORF2** , shows 37% identity to a 6-methylsalicylic acid synthase from Penicillium patulum. Cultures of S. lividans TK24 and S. coelicolor CH999 containing plasmids with **ORF2** on a 5.5-kb PstI fragment were able to produce orsellinic acid, an unreduced version of 6-methylsalicylic acid. The amino acid sequence encoded...

9/3,K/4 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

13446883 PMID: 9128724
The aminonucleoside antibiotic A201A is inactivated by a phosphotransferase activity from Streptomyces capreolus NRRL 3817, the producing organism. Isolation and molecular characterization of the relevant encoding gene and its DNA flanking regions.
Barrasa M I; Tercero J A; Jimenez A
Centro de Biologia Molecular Severo Ochoa (C.S.I.C/U.A.M.), Universidad Autonoma, Madrid, Spain.
European journal of biochemistry / FEBS (GERMANY) Apr 1 1997, 245 (1) p54-63, ISSN 0014-2956 Journal Code: 0107600
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

A novel resistance determinant (ard2) to the aminonucleoside antibiotic A201A was cloned from **Streptomyces** capreolus NRRL 3817, the producing organism, and expressed in **Streptomyces** lividans. Sequencing and subcloning experiments of a 3-kb fragment localized ard2 to an ORF of 591 nucleotides. Cell-free extracts from both S. capreolus...
... incomplete ORFs (2 and 5) and one complete ORF (4), which appear to determine enzymes of the A201A biosynthetic pathway. Whereas the deduced product of **ORF2** did not show any similarity to proteins in data banks,

those of ORF5 and ORF4 encode putative glycosyltransferase and ketoreductase activities, respectively. ard2 and these three ORFs seem to be transcribed in a single polycistronic transcript, which supports the notion that they are a part of an A201A biosynthetic **gene cluster** .

9/3,K/5 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

13357924 PMID: 9031628
Analysis of four tylosin biosynthetic genes from the tylLM region of the Streptomyces fradiae genome.
Gandecha A R; Large S L; Cundliffe E
Department of Biochemistry, University of Leicester, UK.
Gene (NETHERLANDS) Jan 15 1997, 184 (2) p197-203, ISSN 0378-1119 Journal Code: 7706761
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

The tylLM region of the tylosin biosynthetic **gene cluster** of **Streptomyces** fradiae contains four open reading frames (orfs1*-4*). The function of the orf1* product is not known. The product of **orf2** * (tylM2) is the glycosyltransferase that adds mycaminose to the 5-hydroxyl group of tylactone, the polyketide aglycone of tylosin (Ty). A methyltransferase, responsible for 3...

9/3,K/6 (Item 6 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

12728505 PMID: 7649862
Overexpression of a gene cluster **encoding a chalcone synthase-like protein confers redbrown pigment production in Streptomyces griseus.**
Ueda K; Kim K M; Beppu T; Horinouchi S
Department of Biotechnology, University of Tokyo, Japan.
Journal of antibiotics (JAPAN) Jul 1995, 48 (7) p638-46, ISSN 0021-8820 Journal Code: 0151115
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Overexpression of a gene cluster **encoding a chalcone synthase-like protein confers redbrown pigment production in Streptomyces griseus.**
A 7.0-kb DNA fragment that conferred redbrown pigment production on **Streptomyces** griseus was shotgun-cloned with a multicopy vector pIJ486 from this microorganism. By restriction endonuclease mapping and subcloning, a 1.5-kb fragment which is...

... pigment was determined. The nucleotide sequence of this region revealed the presence of two open reading frames, ORF1 with 109 amino acids (named RppA) and **ORF2** with 262 amino acids (RppB), in addition to a truncated ORF3. The termination codon of rppA and the initiation codon of rppB overlapped, sharing one...

... in plants. Part of RppA showed sequence similarity to the 33kDa phosphoprotein of adenovirus. Nucleotide sequences homologous to rppA and rppB were widely distributed in **Streptomyces** species, as determined by Southern hybridization. Further nucleotide sequencing of the entire orf-3 gene showed that ORF3 with 403 amino acids was a cytochrome P-450 (named P-450RPP). These data suggested that the cloned fragment contained part of

a **gene cluster** for the biosynthesis of a certain metabolite. Introduction of the subcloned 1.5-kb fragment into **Streptomyces** lividans as well as Escherichia coli also caused production of redbrown pigment, suggesting that RppA and RppB are capable of synthesizing the redbrown pigment from...

9/3,K/7 (Item 7 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

12644214 PMID: 7768860
A second branched-chain alpha-keto acid dehydrogenase gene cluster **(bkdFGH) from Streptomyces avermitilis: its relationship to avermectin biosynthesis and the construction of a bkdF mutant suitable for the production of novel antiparasitic avermectins.**
Denoya C D; Fedechko R W; Hafner E W; McArthur H A; Morgenstern M R; Skinner D D; Stutzman-Engwall K; Wax R G; Wernau W C
Central Research Division, Pfzer Inc., Groton, Connecticut 06340, USA.
Journal of bacteriology (UNITED STATES) Jun 1995, 177 (12) p3504-11, ISSN 0021-9193 Journal Code: 2985120R
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

A second branched-chain alpha-keto acid dehydrogenase gene cluster **(bkdFGH) from Streptomyces avermitilis: its relationship to avermectin biosynthesis and the construction of a bkdF mutant suitable for the production of novel antiparasitic avermectins.**
... genes encoding the E1 alpha, E1 beta, and E2 subunits of branched-chain alpha-keto acid dehydrogenase (BCDH), bkdFGH, has been cloned and characterized from **Streptomyces** avermitilis, the soil microorganism which produces anthelmintic avermectins. Open reading frame 1 (ORF1) (bkdF, encoding E1 alpha), would encode a polypeptide of 44,394 Da (406 amino acids). The putative start codon of the incompletely sequenced **ORF2** (bkdG, encoding E1 beta) is located 83 bp downstream from the end of ORF1. The deduced amino acid sequence of bkdF resembled the corresponding E1...

9/3,K/8 (Item 8 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10286425 PMID: 7984112
Analysis of five tylosin biosynthetic genes from the tyllBA region of the Streptomyces fradiae genome.
Merson-Davies L A; Cundliffe E
Department of Biochemistry, University of Leicester, UK.
Molecular microbiology (ENGLAND) Jul 1994, 13 (2) p349-55, ISSN 0950-382X Journal Code: 8712028
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

The tyllBA region of the tylosin biosynthetic **gene cluster** of **Streptomyces** fradiae contains at least five open reading frames (ORFs). ORF1 (tylI) encodes a cytochrome P450 and mutations in this gene affect macrolide ring hydroxylation. The product of **ORF2** (tylB) belongs to a widespread family of proteins whose functions are speculative, although tylB mutants are defective in the biosynthesis or addition of mycaminose during...

... deoxyhexose sugars of tylosin via the common intermediate, delta TDP-4-keto, 6-deoxyglucose. ORF5 encodes a thioesterase similar to one encoded in the erythromycin **gene cluster** of Saccharopolyspora erythraea.

9/3,K/9 (Item 9 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10225632 PMID: 7929165
DNA sequence and functions of the actVI region of the actinorhodin biosynthetic gene cluster of Streptomyces coelicolor A3(2).
Fernandez-Moreno M A; Martinez E; Caballero J L; Ichinose K; Hopwood D A; Malpartida F
Centro Nacional de Biotecnologia, Consejo Superior de Investigaciones Cientificas, Campus Universidad Autonoma de Madrid, Spain.
Journal of biological chemistry (UNITED STATES) Oct 7 1994, 269 (40) p24854-63, ISSN 0021-9258 Journal Code: 2985121R
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

DNA sequence and functions of the actVI region of the actinorhodin biosynthetic gene cluster of Streptomyces coelicolor A3(2).
... sequencing of 5.7 kilobase pairs at the left end of the act cluster (the so-called "actVI region"), in the order: ORFB, ORFA, ORF1, **ORF2** , ORF3, ORF4. ORF1-4 are transcribed rightward and in the same direction as the ORFs of the actVA region which lies to the right of...
... using phi C31 derivatives, did not cause any obvious change in actinorhodin production, defects in actinorhodin synthesis were obtained by insertional inactivation of ORFA, ORF1, **ORF2** , or ORF3. RNA analysis within the ORF1/ORFA intergenic region showed overlapping divergent promoters, at least one of which is under the control of the...

...show any significant similarities with other known proteins. The deduced product of ORFA strongly resembles those of genes of unknown function from Saccharopolyspora hirsuta and **Streptomyces** roseofulvus, located within polyketide synthase clusters. The ORF1 product strongly resembles beta-hydroxyacyl-CoA dehydrogenases of bacteria and mammals and the **ORF2** and ORF4 products resemble each other and enoyl reductases from bacteria, animals, and plants, with a highly conserved cofactor-binding domain. These findings strongly suggest...

9/3,K/10 (Item 10 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10056475 PMID: 8169211
Cloning, sequencing, and analysis of the griseusin polyketide synthase gene cluster **from Streptomyces griseus.**
Yu T W; Bibb M J; Revill W P; Hopwood D A
John Innes Institute, John Innes Centre, Norwich, United Kingdom.
Journal of bacteriology (UNITED STATES) May 1994, 176 (9) p2627-34, ISSN 0021-9193 Journal Code: 2985120R
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Cloning, sequencing, and analysis of the griseusin polyketide synthase gene cluster **from Streptomyces griseus.**
A fragment of DNA was cloned from the **Streptomyces** griseus K-63 genome

by using genes (act) for the actinorhodin polyketide synthase (PKS) of **Streptomyces** coelicolor as a probe. Sequencing of a 5.4-kb segment of the cloned DNA revealed a set of five gris open reading frames (ORFs), corresponding to the act PKS genes, in the following order: ORF1 for a ketosynthase, **ORF2** for a chain length-determining factor, ORF3 for an acyl carrier protein, ORF5 for a ketoreductase, and ORF4 for a cyclase-dehydrase. Replacement of the...

9/3,K/11 (Item 11 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09897496 PMID: 8244027
Characterization of a Streptomyces antibioticus gene cluster **encoding a glycosyltransferase involved in oleandomycin inactivation.**
Hernandez C; Olano C; Mendez C; Salas J A
Departamento de Biologia Funcional, (Area Microbiologia), Universidad de Oviedo, Spain.
Gene (NETHERLANDS) Nov 30 1993, 134 (1) p139-40, ISSN 0378-1119 Journal Code: 7706761
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Characterization of a Streptomyces antibioticus gene cluster **encoding a glycosyltransferase involved in oleandomycin inactivation.**
By homology to the mgt gene (encoding a macrolide glycosyltransferase) from **Streptomyces** lividans, a 3.3-kb DNA fragment from the oleandomycin producer, **Streptomyces** antibioticus, was cloned and sequenced. Analysis of the sequence revealed the presence of the 3' end of a gene (ORF1) and two complete ORFs (**ORF2** and oleD), all of them translationally coupled. The deduced product of the sequenced region of ORF1 contained the typical signature of integral membrane proteins responsible for the translocation of substrates across the membrane. The **ORF2** product did not show significant similarity with proteins in databases, but contains an N-terminus leader peptide region characteristic of secreted proteins, and a lipid...

9/3,K/12 (Item 12 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09654463 PMID: 8458843
A gene cluster **involved in aerial mycelium formation in Streptomyces griseus encodes proteins similar to the response regulators of two-component regulatory systems and membrane translocators.**
Ueda K; Miyake K; Horinouchi S; Beppu T
Department of Agricultural Chemistry, Faculty of Agriculture, University of Tokyo, Japan.
Journal of bacteriology (UNITED STATES) Apr 1993, 175 (7) p2006-16, ISSN 0021-9193 Journal Code: 2985120R
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

A gene cluster **involved in aerial mycelium formation in Streptomyces griseus encodes proteins similar to the response regulators of two-component regulatory systems and membrane translocators.**
Mutants of **Streptomyces** griseus deficient in A-factor production are sporulation negative, since A-factor is an essential hormonal regulator for the induction of morphological and physiological differentiation...

... griseus HH1, was cloned from this mutant strain. Subcloning experiments and nucleotide sequencing showed that two open reading frames, ORF1 with 656 amino acids and **ORF2** with 201 amino acids, were required in order to induce sporulation. The amino acid sequence of ORF1 significantly resembled that of the Escherichia coli HlyB...

... a transcriptional unit with an additional upstream gene encoding ORF3, which was greatly similar to ORF1 in size and amino acid sequence. The other protein, **ORF2** , showed significant end-to-end homology with the E. coli uhpA product, a regulatory protein for the uptake of sugar phosphates. Like UhpA as a response regulator of a bacterial two-component regulatory system, **ORF2** contained a helix-turn-helix DNA-binding domain at its COOH-terminal portion and an Asp residue (Asp-54) probably to be phosphorylated at its NH2-terminal portion. An amino acid replacement from Asp-54 to Asn resulted in the loss of the ability of **ORF2** to induce sporulation in strain HH1.

9/3,K/13 (Item 13 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09438597 PMID: 1527048
Nucleotide sequence and deduced functions of a set of cotranscribed genes of Streptomyces coelicolor A3(2) including the polyketide synthase for the antibiotic actinorhodin.
Fernandez-Moreno M A; Martinez E; Boto L; Hopwood D A; Malpartida F
Centro Nacional de Biotecnologia, Madrid, Spain.
Journal of biological chemistry (UNITED STATES) Sep 25 1992, 267 (27) p19278-90, ISSN 0021-9258 Journal Code: 2985121R
Contract/Grant No.: GM 39784; GM; NIGMS
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

A 5.3-kb region of the **Streptomyces** coelicolor actinorhodin **gene cluster** , including the genes for polyketide biosynthesis, was sequenced. Six identified open reading frames (ORF1-6) were related to genetically characterized mutations of classes actI, VII...

...genetical, biochemical, and similarity data, the potential activities of the products of the six genes can be postulated as: 1) condensing enzyme/acyl transferase (ORF1 + **ORF2**); 2) acyl carrier protein (ORF3); 3) putative cyclase/dehydrase (ORF4); 4) dehydrase (ORF5); and 5) "dimerase" (ORF6). The data show that the actinorhodin PKS consists...

9/3,K/14 (Item 14 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09411477 PMID: 1508151
Characterisation of actI-homologous DNA encoding polyketide synthase genes from the monensin producer Streptomyces cinnamonensis.
Arrowsmith T J; Malpartida F; Sherman D H; Birch A; Hopwood D A; Robinson J A
John Innes Institute, Norwich, UK.
Molecular & general genetics - MGG (GERMANY) Aug 1992, 234 (2) p254-64, ISSN 0026-8925 Journal Code: 0125036
Contract/Grant No.: GM39784; GM; NIGMS
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Cloned DNA encoding polyketide synthase (PKS) genes from one **Streptomyces** species was previously shown to serve as a useful hybridisation probe for the isolation of other PKS gene clusters from the same or different species. In this work, the actI and actIII genes, encoding components of the actinorhodin PKS of **Streptomyces** coelicolor, were used to identify and clone a region of homologous DNA from the monensin-producing organism S. cinnamonensis. A 4799 bp fragment containing the...

...and whiE PKS gene clusters. This allowed the assignment of the following putative functions to these five ORFS: a heterodimeric beta-ketoacyl synthase (ORF1 and **ORF2**), an acyl carrier protein (ORF3), a beta-ketoacyl reductase (ORF5), and a bifunctional cyclase/dehydrase (ORF4). The ORFs are encoded in the order ORF1- **ORF2** -ORF3-ORF5-ORF4, and ORFs-1 and -2 show evidence for translational coupling. This act-homologous region therefore appears to encode a PKS **gene cluster** . A gene disruption experiment using the vector pGM160, and other evidence, suggests that this cluster is not essential for monensin biosynthesis but rather is involved...

9/3,K/15 (Item 15 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09152776 PMID: 1766437
Organisation and functions of the actVA region of the actinorhodin biosynthetic gene cluster of Streptomyces coelicolor.
Caballero J L; Martinez E; Malpartida F; Hopwood D A
John Innes Institute, John Innes Centre, Norwich, UK.
Molecular & general genetics - MGG (GERMANY) Dec 1991, 230 (3) p401-12, ISSN 0026-8925 Journal Code: 0125036
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Organisation and functions of the actVA region of the actinorhodin biosynthetic gene cluster of Streptomyces coelicolor.
Sequence analysis of the actVA region of the actinorhodin biosynthetic **gene cluster** of **Streptomyces** coelicolor revealed a succession of six open reading frames (ORFs), all running in the same direction and extending over 5.32 kb. The protein product of actVA-ORF1 strongly resembles that of another gene, elsewhere in the act cluster (actII- **ORF2**), which codes for a trans-membrane protein previously implicated in actinorhodin export from the mycelium. This suggests that the two gene products may co-operate... ... mapping of actVA mutants to actVA-ORF3 and -ORF5 (and perhaps -ORF4), and by the finding of strong resemblances between the protein products of actVA- **ORF2** and -ORF6 and the products of genes of the oxytetracycline or tetracenomycin gene clusters that have been implicated in ring-hydroxylation reactions in the biosynthesis...

9/3,K/16 (Item 16 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09034766 PMID: 1716725
Transcriptional organization and regulation of an antibiotic export complex in the producing Streptomyces culture.
Caballero J L; Malpartida F; Hopwood D A
John Innes Institute, John Innes Centre, Norwich, UK.
Molecular & general genetics - MGG (GERMANY) Sep 1991, 228 (3) p372-80, ISSN 0026-8925 Journal Code: 0125036
Document type: Journal Article

Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Three open reading frames (ORFs) in the actII region of the actinorhodin biosynthetic **gene cluster** of **Streptomyces** coelicolor A3(2), which are involved in the export of the antibiotic are carried on two divergent transcripts. A monocistronic transcript carries actII-ORF1, encoding a putative repressor protein, and a bicistronic transcript codes for actII-**ORF2** and -ORF3, whose products have been postulated to form an antibiotic export complex. The actII-ORF1 and actII- **ORF2** /3 transcripts each have a single promoter and the promoters for the two transcripts overlap. Both promoters are most active in cultures that have developed to the stage of actinorhodin production. The promoters resemble consensus promoters of the vegetative class in Escherichia coli and **Streptomyces** . We also demonstrate that these promoters are expressed in E. coli and use this finding to reveal a regulatory role for the repressor, using the xylE reporter gene on promoter-probe shuttle vectors and regulated expression of the actII-ORF1 gene under control of Plac. The actII- **ORF2** /3 promoter is strongly repressed by the ORF1 product and the ORF1 product also represses its own promoter. The finding that the operator/promoter arrangement, and regulatory interconnection, of an antibiotic export/repressor gene pair in **Streptomyces** strikingly resemble those for tetracycline resistance in bacteria of clinical importance supports the hypothesis of an evolutionary origin of such genes in an ancestral actinomycete.

9/3,K/17 (Item 17 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08340135 PMID: 2684656
Analysis of the nucleotide sequence of the Streptomyces glaucescens tcmI genes provides key information about the enzymology of polyketide antibiotic biosynthesis.
Bibb M J; Biro S; Motamedi H; Collins J F; Hutchinson C R
John Innes Institute, Norwich, UK.
EMBO journal (ENGLAND) Sep 1989, 8 (9) p2727-36, ISSN 0261-4189
Journal Code: 8208664
Contract/Grant No.: CA 35381; CA; NCI
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Key information about the biosynthesis of polyketide metabolites has been uncovered by sequence analysis of the tetracenomycin C polyketide synthase genes (tcmI) from **Streptomyces** glaucescens GLA.0. The sequence data revealed the presence of three complete open reading frames (ORFs). ORF1 and **ORF2** appear to be translationally coupled and would encode proteins containing 426 and 405 amino acids, respectively. The two deduced proteins are homologous to known beta-ketoacyl synthases. ORF3 begins 70 nucleotides after the stop codon of **ORF2** and would code for an 83 amino acid protein with a strong resemblance to known bacterial, animal and plant acyl-carrier proteins (ACP). The presence of an ACP gene within the tcm **gene cluster** suggests that different ACPs are used in fatty acid and polyketide biosynthesis in **Streptomyces** . We conclude from these data and earlier information that polyketide biosynthesis in S. glaucescens, and most likely in other bacteria, involves a multienzyme complex consisting...

9/3,K/18 (Item 18 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08340134 PMID: 2583128
Structure and deduced function of the granaticin-producing polyketide synthase gene cluster of Streptomyces violaceoruber Tu22.
Sherman D H; Malpartida F; Bibb M J; Kieser H M; Bibb M J; Hopwood D A
John Innes Institute, Norwich, UK.
EMBO journal (ENGLAND) Sep 1989, 8 (9) p2717-25, ISSN 0261-4189
Journal Code: 8208664
Contract/Grant No.: GM39784-02; GM; NIGMS
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Structure and deduced function of the granaticin-producing polyketide synthase gene cluster of Streptomyces violaceoruber Tu22.
A 6.5 kb region of DNA from **Streptomyces** violaceoruber, which contains polyketide synthase (PKS) genes for production of the benzoisochromane quinone moiety of the antibiotic, granaticin, was cloned and sequenced. Of six open...

... ORFs) identified, four (ORFs 1-4) would be transcribed in one direction and two (ORFs 5 and 6) divergently from ORFs 1-4. ORF1 and **ORF2** , which show evidence for translation coupling, encode (deduced) gene products which strongly resemble each other and the Escherichia coli fatty acid ketoacyl synthase (condensing enzyme...

... conclude that ORF1 (which contains a characteristic cysteine residue) functions as a condensing enzyme, possibly as part of a heterodimeric protein including the product of **ORF2** . The predicted ORF3 gene product strikingly resembles acyl carrier proteins (ACPs) of fatty acid synthase (FAS), particularly in the region of the active site motif...

9/3,K/19 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0011252756 BIOSIS NO.: 199800047003
Cloning and expression of a gene from Streptomyces scabies encoding a putative pathogenicity factor
AUTHOR: Bukhalid Raghida A; Loria Rosemary (Reprint)
AUTHOR ADDRESS: Dep. Plant Pathol., Cornell Univ., 334 Plant Sci. Build., Ithaca, NY 14853-4203, USA**USA
JOURNAL: Journal of Bacteriology 179 (24): p7776-7783 Dec., 1997 1997
MEDIUM: print
ISSN: 0021-9193
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: We cloned a 9.4-kb DNA fragment from **Streptomyces** scabies ATCC 41973 that allows the nonpathogen **Streptomyces** lividans 66 TK24 to necrotize and colonize potato tuber slices and produce scab-like symptoms on potato minitubers. Deletion analysis demonstrated that activity was conferred...

...of the IS1164 elements from Rhodococcus rhodochrous (71%) and Mycobacterium bovis (68%), members of the Staphylococcus aureus IS256 family of transposases. No significant homologies to **ORF2** and ORF3 were found in the nucleic acid and protein databases. ORFtnp is located 5' of ORF3. **ORF2** is incomplete and is located 3' of ORF3. Subcloning of the individual ORFs demonstrated that ORF3, designated nec1, is sufficient for necrotizing activity in S...

...of nec1 suggests that it has moved horizontally from another genus.

Southern analysis of ORFtnp and nec1 demonstrate that these genes are physically linked in **Streptomyces** strains, including S. scabies and **Streptomyces** acidiscabies strains, that are pathogenic on potato and that produce the phytotoxin thaxtomin A. These data suggest that nec1 may have been mobilized into S...
DESCRIPTORS:
MISCELLANEOUS TERMS: **gene cloning** ;

9/3,K/20 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
(c) 2004 BIOSIS. All rts. reserv.

0009426863 BIOSIS NO.: 199497448148
Analysis of five tylosin biosynthetic genes from the tyIIBA region of the Streptomyces fradiae genome
AUTHOR: Merson-Davies Louise A; Cundliffe Eric (Reprint)
AUTHOR ADDRESS: Dep. Biochem., Univ. Leicester, Leicester LE1 7RH, UK**UK
JOURNAL: Molecular Microbiology 13 (2): p349-355 1994 1994
ISSN: 0950-382X
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The tyIIBA region of the tylosin biosynthetic **gene cluster** of **Streptomyces** fradiae contains at least five open reading frames (ORFs). ORF1 (tyII) encodes a cytochrome P450 and mutations In this gene affect macrolide ring hydroxylation. The product of **ORF2** (tyIB) belongs to a widespread family of proteins whose functions are speculative, although tyIB mutants are defective In the biosynthesis or addition of mycaminose during...

...three deoxyhexose sugars of tylosin via the common Intermediate, delta-TDP4-keto, 6-deoxyglucose. ORF5 encodes a thioesterase similar to one encoded in the erythromycin **gene cluster** of Saccharopolyspore erythraea.
DESCRIPTORS:
MISCELLANEOUS TERMS: ... **GENE CLUSTER** ;

9/3,K/21 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
(c) 2004 BIOSIS. All rts. reserv.

0006792035 BIOSIS NO.: 198988107150
ANALYSIS OF THE NUCLEOTIDE SEQUENCE OF THE STREPTOMYCES-GLAUCESCENS TCML GENES PROVIDES KEY INFORMATION ABOUT THE ENZYMOLOGY OF POLYKETIDE ANTIBIOTIC BIOSYNTHESIS
AUTHOR: BIBB M J (Reprint); BIRO S; MOTAMEDI H; COLLINS J F; HUTCHINSON C R
AUTHOR ADDRESS: JOHN INNES INST, COLNEY LANE, NORWICH NR4 7UH, UK**UK
JOURNAL: EMBO (European Molecular Biology Organization) Journal 8 (9): p 2727-2736 1989
ISSN: 0261-4189
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Key information about the biosynthesis of polyketide metabolites has been uncovered by sequence analysis of the tetracenomycin C polyketide synthase genes (tcmI) from **Streptomyces** glaucescens GLA.O. The sequence data revealed the presence of three complete open reading frames (ORFs). ORF1 and **ORF2** appear to be translationally coupled and would encode proteins containing 426 and 405 amino acids, respectively. The two deduced proteins are homologous to known .beta.-ketoacyl synthases. ORF3 begins 70 nucleotides after the stop codon of **ORF2** and

would code for an 83 amino acid protein with a strong resemblance to known bacterial, animal and plant acyl-carrier proteins (ACP). The presence of an ACP gene within the tcm **gene cluster** suggests that different ACPs are used in fatty acid and polyketide biosynthesis in **Streptomyces** . We conclude from these data and earlier information that polyketide biosynthesis in S. glaucescens, and most likely in other bacteria, involves a multienzyme complex consisting...

9/3,K/22 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE
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05979282 EMBASE No: 1995006455
Cloning and sequencing of a cluster of genes encoding branched-chain alpha- keto acid dehydrogenase from Streptomyces avermitilis and the production of a functional E1(alphabeta) component in Escherichia coli
Skinner D.D.; Morgenstern M.R.; Fedechko R.W.; Denoya C.D.
Pfizer Inc., Bioprocess Research,Groton, CT 06340 United States
Journal of Bacteriology (J. BACTERIOL.) (United States) 1995, 177/1 (183-190)
CODEN: JOBAA ISSN: 0021-9193
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

A cluster of genes encoding the E1alpha, E1beta, and E2 subunits of branched- chain alpha-keto acid dehydrogenase (BCDH) of **Streptomyces** avermitilis has been cloned and sequenced. Open reading frame 1 (ORF1) (E1alpha), 1,146 nucleotides long, would encode a polypeptide of 40,969 Da (381 amino acids). **ORF2** (E1beta), 1,005 nucleotides long, would encode a polypeptide of 35,577 Da (334 amino acids). The intergenic distance between ORF1 and **ORF2** is 73 bp. The putative ATG start codon of the incomplete ORF3 (E2) overlaps the stop codon of **ORF2** . Computer-aided searches showed that the deduced products of ORF1 and **ORF2** resembled the corresponding E1 subunit (alpha or beta) of several prokaryotic and eukaryotic BCDH complexes. When these ORFs were overexpressed in Escherichia coli, proteins of about 41 and 34 kDa, which are the approximate masses of the predicted S. avermitilis ORF1 and **ORF2** products, respectively, were detected. In addition, specific E1(alphabeta) BCDH activity was detected in E. coli cells carrying the S. avermitilis ORF1 (E1alpha) and **ORF2** (E1beta) coexpressed under the control of the T7 promoter.
MEDICAL DESCRIPTORS:
amino acid sequence; article; bacterial genetics; dna sequence; **gene cluster** ; gene mapping; molecular cloning; nonhuman; open reading frame; plasmid; polymerase chain reaction; priority journal; sequence homology; southern blotting

9/3,K/23 (Item 2 from file: 73)
DIALOG(R)File 73:EMBASE
(c) 2004 Elsevier Science B.V. All rts. reserv.

05904566 EMBASE No: 1994310776
Isolation and sequence analysis of polyketide synthase genes from the daunomycin-producing Streptomyces sp. strain C5
Ye J.; Dickens M.L.; Plater R.; Li Y.; Lawrence J.; Strohl W.R.
Department of Microbiology, Ohio State University, 484 West 12th Ave.,Columbus, OH 43210-1292 United States
Journal of Bacteriology (J. BACTERIOL.) (United States) 1994, 176/20 (6270-6280)
CODEN: JOBAA ISSN: 0021-9193
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

A contiguous region of about 30 kbp of DNA putatively encoding reactions

in daunomycin biosynthesis was isolated from **Streptomyces** sp. strain C5 DNA. The DNA sequence of an 8.1-kbp EcoRI fragment, which hybridized with actI polyketide synthase (PKS) and actIII polyketide reductase...

...The five latter genes encode: (i) a homolog of TcmH, an oxygenase of the tetracenomycin biosynthesis pathway; (ii) a PKS Orf1 homolog; (iii) a PKS **Orf2** homolog (chain length factor); (iv) a product having moderate sequence identity with Escherichia coli beta-ketoacyl acyl carrier protein synthase III but lacking the conserved...

...highly similar to several acyltransferases. The DNA within the 8.1-kbp EcoR1 fragment restored daunomycin production to two dauA non-daunomycin-producing mutants of **Streptomyces** sp. strain C5 and restored wild-type antibiotic production to **Streptomyces** coelicolor B40 (actVII; nonfunctional cyclase/dehydrase), and to S. coelicolor B41 (actIII) and **Streptomyces** galilaeus ATCC 31671, strains defective in PKR activity.
MEDICAL DESCRIPTORS:
amino acid sequence; article; controlled study; **gene cluster** ; gene isolation; gene sequence; nonhuman; open reading frame; priority journal; restriction mapping; sequence homology; streptomyces coelicolor

9/3,K/24 (Item 3 from file: 73)
DIALOG(R)File 73:EMBASE

05437521 EMBASE No: 1993205620
Saccharopolyspora hirsuta 367 encodes clustered genes similar to ketoacyl synthase, ketoacyl reductase, acyl carrier protein, and biotin carboxyl carrier protein
Le Gouill C.; Desmarais D.; Dery C.V.
Departement de Biologie, Faculte de Sherbrooke, Universite de Sherbrooke,Sherbrooke, Que. J1K 2R1 Canada
Molecular and General Genetics (MOL. GEN. GENET.) (Germany) 1993, 240/1 (146-150)
CODEN: MGGEA ISSN: 0026-8925
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

The actI gene, encoding a component of the actinorhodin polyketide synthase of **Streptomyces** coelicolor, was used to identify and clone a homologous 11.7 kb BamHI DNA fragment from Saccharopolyspora hirsuta 367. The cloned fragment complemented actinorhodin production in a strain of **Streptomyces** coelicolor bearing a mutant actI gene. The DNA sequence of a 5.1 kb fragment revealed 6 open reading frames (ORF). ORF1 does not resemble any known DNA or deduced protein sequence, while the deduced protein sequence of **ORF2** resembles that of biotin carboxyl carrier proteins. Based on the similarity to deduced protein sequences from cloned genes of polyketide producers, ORF3 would code for...
MEDICAL DESCRIPTORS:
*amino acid sequence; * **gene cluster** ; *gene structure; *nucleotide sequence

9/3,K/25 (Item 4 from file: 73)
DIALOG(R)File 73:EMBASE

05159238 EMBASE No: 1992299471
Functional replacement of genes for individual polyketide synthase components in Streptomyces coelicolor A3(2) by heterologous genes from a different polyketide pathway
Sherman D.H.; Kim E.-S.; Bibb M.J.; Hopwood D.A.
Department of Microbiology, Biological Process Technology Inst.,

University of Minnesota, 1479 Gortner Avenue,St. Paul, MN 55108 United States
Journal of Bacteriology (J. BACTERIOL.) (United States) 1992, 174/19 (6184-6190)
CODEN: JOBAA ISSN: 0021-9193
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Streptomyces coelicolor A3(2) and **Streptomyces** violaceoruber Tu22 produce the antibiotics actinorhodin and granaticin, respectively. Both the aglycone of granaticin and the half-molecule of actinorhodin are derived from one acetyl...

...open reading frames (ORFs) in the actI region had been altered in each of a set of 13 actI mutants. It also proved that actI- **ORF2** (whose putative protein product shows overall similarity to the beta-ketoacyl synthase encoded by actI-ORF1 but whose function is unclear) is essential for PKS function. Mutations in each of the four complemented act genes (actI-ORF1, actI- **ORF2** , actIII, and actVII) were cloned and sequenced, revealing a nonsense or frameshift mutation in each mutant.
MEDICAL DESCRIPTORS:
article; bacterium mutant; enzyme activity; **gene cluster** ; gene sequence ; gene structure; genetic analysis; genetic complementation; metabolism; molecular cloning; nonhuman; open reading frame; plasmid; priority journal; stereochemistry

```
?

Set     Items   Description
S1          0   ORF2 (S) (CLAVULANIC)
S2        214   ORF2 (S) (STREPTOMYCES)
S3          0   S2 AND (CLAVULANIC (W) ACID)
S4        274   (CLAVULANIC) (S) (STREPTOMYCES)
S5          0   S4 AND ORF2
S6          0   S2 AND S4
S7         81   S2 AND (GENE (W) (CLUSTER OR CLONING))
S8         35   RD (unique items)
S9         25   S8 NOT PY>1999
?
S CLAVULANIC (S) (BIOSYNTHESIS OR PRODUCTION)
          21765  CLAVULANIC
         701830  BIOSYNTHESIS
        1272039  PRODUCTION
    S10     851  CLAVULANIC (S) (BIOSYNTHESIS OR PRODUCTION)
?
S S10 AND S4
            851  S10
            274  S4
    S11     217  S10 AND S4
?

Set     Items   Description
S1          0   ORF2 (S) (CLAVULANIC)
S2        214   ORF2 (S) (STREPTOMYCES)
S3          0   S2 AND (CLAVULANIC (W) ACID)
S4        274   (CLAVULANIC) (S) (STREPTOMYCES)
S5          0   S4 AND ORF2
S6          0   S2 AND S4
S7         81   S2 AND (GENE (W) (CLUSTER OR CLONING))
S8         35   RD (unique items)
S9         25   S8 NOT PY>1999
S10       851   CLAVULANIC (S) (BIOSYNTHESIS OR PRODUCTION)
S11       217   S10 AND S4
?
S S11 AND (PLASMID OR VECTOR)
            217  S11
```

```
          189675  PLASMID
          276160  VECTOR
     S12       20  S11 AND (PLASMID OR VECTOR)
?
RD
...completed examining records
     S13       11  RD (unique items)
?
T S13/3,K/ALL
```

13/3,K/1 (Item 1 from file: 155)

16305114 PMID: 15150229

Two oligopeptide-permease-encoding genes in the clavulanic **acid cluster of** Streptomyces **clavuligerus are essential for** production □of the□ **beta-lactamase inhibitor.**

Lorenzana Luis M; Perez-Redondo Rosario; Santamarta Irene; Martin Juan F; Liras Paloma

Area de Microbiologia, Facultad de Ciencias Biologicas y Ambientales, University of Leon, 24071 Leon, Spain.

Journal of bacteriology (United States) Jun 2004, 186 (11) p3431-8, ISSN 0021-9193 Journal Code: 2985120R

Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Two oligopeptide-permease-encoding genes in the clavulanic **acid cluster of** Streptomyces **clavuligerus are essential for** production □of the□ **beta-lactamase inhibitor.**

orf7 (oppA1) and orf15 (oppA2) are located 8 kb apart in the **clavulanic** acid gene cluster of **Streptomyces** clavuligerus and encode proteins which are 48.0% identical. These proteins show sequence similarity to periplasmic oligopeptide-binding proteins. Mutant S. clavuligerus oppA1::acc, disrupted in oppA1, lacks **clavulanic** acid **production** . □Clavulanic□ acid **production** is restored by transformation with **plasmid** pIJ699-oppA1, which carries oppA1, but not with the multicopy **plasmid** pIJ699-oppA2, which carries oppA2. The mutant S. clavuligerus oppA2::aph also lacks **clavulanic** acid **production** , shows a bald phenotype, and overproduces holomycin (5). **Clavulanic** acid **production** at low levels is restored in the oppA2-disrupted mutants by transformation with **plasmid** pIJ699-oppA2, but it is not complemented by the multicopy **plasmid** pIJ699-oppA1. Both genes encode oligopeptide permeases with different substrate specificities. The disrupted S. clavuligerus oppA2::aph is not able to grow on RPPGFSPFR (Arg...

Descriptors: Bacterial Proteins--genetics--GE; * **Clavulanic** Acid--**biosynthesis** --BI; *Enzyme Inhibitors--metabolism--ME; *Membrane Transport Proteins--genetics--GE; *Multigene Family; *Streptomyces--genetics--GE; *beta-Lactamases--antagonists and inhibitors--AI

13/3,K/2 (Item 2 from file: 155)

13991843 PMID: 9689037

beta-Lactam synthetase: a new biosynthetic enzyme.

Bachmann B O; Li R; Townsend C A

Department of Chemistry, The Johns Hopkins University, 3400 North Charles Street, Baltimore, MD 21218, USA.

Proceedings of the National Academy of Sciences of the United States of America (UNITED STATES) Aug 4 1998, 95 (16) p9082-6, ISSN 0027-8424 Journal Code: 7505876

Contract/Grant No.: AI 14937; AI; NIAID
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

The principal cause of bacterial resistance to penicillin and other beta-lactam antibiotics is the acquisition of **plasmid** -encoded beta-lactamases, enzymes that catalyze hydrolysis of the beta-lactam bond and render these antibiotics inactive. **Clavulanic** acid is a potent inhibitor of beta-lactamases and has proven clinically effective in combating resistant infections. Although **clavulanic** acid and penicillin share marked structural similarities, the biosyntheses of their bicyclic nuclei are wholly dissimilar. In contrast to the efficient iron-mediated oxidative cyclization of a tripeptide to isopenicillin N, the critical beta-lactam ring of **clavulanic** acid is demonstrated to form by intramolecular closure catalyzed by a new type of ATP/Mg2+-dependent enzyme, a beta-lactam synthetase (beta-LS). Insertional inactivation of its encoding gene in wild-type **Streptomyces** clavuligerus resulted in complete loss of **clavulanic** acid **production** and the accumulation of N2-(carboxyethyl)-L-arginine (CEA). Chemical complementation of this blocked mutant with authentic deoxyguanidinoproclavaminic acid (DGPC), the expected product of the beta-LS, restored **clavulanic** acid synthesis. Finally, overexpression of this gene gave the beta-LS, which was shown to mediate the conversion of CEA to DGPC in the presence...
Descriptors: Amidohydrolases--metabolism--ME; *Anti-Bacterial Agents --biosynthesis--BI; **Clavulanic** Acid- **biosynthesis** --BI

13/3,K/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

12542586 PMID: 7876185
Expression and purification of two isozymes of clavaminate synthase and initial characterization of the iron binding site. General error analysis in polymerase chain reaction amplification.
Busby R W; Chang M D; Busby R C; Wimp J; Townsend C A
Department of Chemistry, Johns Hopkins University, Baltimore, Maryland 21218.
Journal of biological chemistry (UNITED STATES) Mar 3 1995, 270 (9) p4262-9, ISSN 0021-9258 Journal Code: 2985121R
Contract/Grant No.: AI14937; AI; NIAID
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Clavaminate synthase is an Fe(2+)-, O2-, and alpha-ketoglutarate-dependent oxygenase that catalyzes three transformations in the **biosynthesis** of the important beta-lactamase inhibitor **clavulanic** acid. The genes from **Streptomyces** clavuligerus encoding two isoenzymes of clavaminate synthase have been over-expressed in Escherichia coli to give soluble proteins whose reactions, kinetic properties, and molecular masses...

... presence of histidine and cysteine, respectively, at or near the active site and possibly involved in iron binding. In the course of constructing the expression **vector** , a simply applied general error analysis of the polymerase chain reaction was formulated to calculate the proportion of correctly replicated DNA and guide the design...

13/3,K/4 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

11815112 PMID: 12003953
CcaR is an autoregulatory protein that binds to the ccaR and cefD-cmcI promoters of the cephamycin C- clavulanic **acid cluster in** Streptomyces **clavuligerus.**
Santamarta Irene; Rodriguez-Garcia Antonio; Perez-Redondo Rosario; Martin Juan F; Liras Paloma
Area de Microbiologia, Facultad de Ciencias Biologicas y Ambientales, Universidad de Leon, 24071 Leon, Spain.
Journal of bacteriology (United States) Jun 2002, 184 (11) p3106-13, ISSN 0021-9193 Journal Code: 2985120R
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

CcaR is an autoregulatory protein that binds to the ccaR and cefD-cmcI promoters of the cephamycin C- clavulanic **acid cluster in** Streptomyces **clavuligerus.**
The putative regulatory CcaR protein, which is encoded in the beta-lactam supercluster of **Streptomyces** clavuligerus, has been partially purified by ammonium sulfate precipitation and heparin affinity chromatography. In addition, it was expressed in Escherichia coli, purified as a His...

... the bidirectional cefD-cmcI promoter region. In contrast, CcaR did not bind to DNA fragments with the promoter regions of other genes of the cephamycin- **clavulanic** acid supercluster including lat, blp, claR, car-cyp, and the unlinked argR gene. The DNA shifts obtained with CcaR were prevented by anti-rCcaR immunoglobulin...

... but not by anti-rabbit IgG antibodies. ccaR and the bidirectional cefD-cmcI promoter region were fused to the xylE reporter gene and expressed in **Streptomyces** lividans and S. clavuligerus. These constructs produced low catechol dioxygenase activity in the absence of CcaR; activity was increased 1.7- to 4.6-fold in cultures expressing CcaR. Amplification of the ccaR promoter region lacking its coding sequence in a high-copy-number **plasmid** in S. clavuligerus ATCC 27064 resulted in a reduced **production** of cephamycin C and **clavulanic** acid, by 12 to 20% and 40 to 60%, respectively, due to titration of the CcaR regulator. These findings confirm that CcaR is a positively...
; Amino Acid Isomerases--metabolism--ME; **Clavulanic** Acid-- **biosynthesis** --BI; DNA-Binding Proteins--isolation and purification--IP; DNA-Binding Proteins--metabolism--ME; Genes, Bacterial; Genes, Regulator; Promoter Regions (Genetics); Recombinant Fusion Proteins--metabolism--ME...

13/3,K/5 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09790940 PMID: 8349096
The biosynthetic genes for clavulanic **acid and cephamycin** production **occur as a 'super-cluster' in three** Streptomyces .
Ward J M; Hodgson J E
SmithKline Beecham Pharmaceuticals, Brockham Park Research Centre, Betchworth, Surrey, UK.
FEMS microbiology letters (NETHERLANDS) Jun 15 1993, 110 (2) p239-42, ISSN 0378-1097 Journal Code: 7705721
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

The biosynthetic genes for clavulanic **acid and cephamycin** production

occur as a 'super-cluster' in three Streptomyces .
The cosmid cloning **vector** pHC79 has been used to clone fragments of chromosomal DNA from the **Streptomyces** : S. clavuligerus, S. jumonjinensis and S. katsurahamanus. These strains all produce both the beta-lactam antibiotic, cephamycin and the beta-lactamase inhibitor, **clavulanic** acid. Although structurally related these two beta-lactams are known to be derived from different biosynthetic precursors. Hybridisation studies and restriction mapping have shown that the gene clusters encoding the two biosynthetic pathways are chromosomally adjacent in these strains, thus creating a 'super-cluster' of genes involved in both the **production** and enhancement of activity of a beta-lactam antibiotic.
Descriptors: Bacterial Proteins--genetics--GE; *Cephamycins--biosynthesis --BI; * **Clavulanic** Acids-- **biosynthesis** --BI; *Genes, Structural, Bacterial; *Intramolecular Transferases; *Isomerases--genetics--GE; *Mixed Function Oxygenases--genetics--GE; *Multigene Family; *Streptomyces --genetics--GE

13/3,K/6 (Item 6 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09361783 PMID: 1339424
Characterization of the Streptomyces **clavuligerus argC gene encoding N-acetylglutamyl-phosphate reductase: expression in** Streptomyces **lividans and effect on** clavulanic **acid** production□.□
Ludovice M; Martin J F; Carrachas P; Liras P
Area of Microbiology, Faculty of Biology, University of Leon, Spain.
Journal of bacteriology (UNITED STATES) Jul 1992, 174 (14) p4606-13, ISSN 0021-9193 Journal Code: 2985120R
Document type: Journal Article
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Characterization of the Streptomyces **clavuligerus argC gene encoding N-acetylglutamyl-phosphate reductase: expression in** Streptomyces **lividans and effect on** clavulanic **acid** production□.□
The argC gene of **Streptomyces** clavuligerus encoding N-acetylglutamyl-phosphate reductase (AGPR) has been cloned by complementation of argC mutants **Streptomyces** lividans 1674 and Escherichia coli XC33. The gene is contained in an open reading frame of 1,023 nucleotides which encodes a protein of 340...
... AGPR is repressed by addition of arginine to the culture medium. The protein encoded by the argC gene is very similar to the AGPRs of **Streptomyces** coelicolor, Bacillus subtilis, and E. coli and, to a lesser degree, to the homologous enzymes of Saccharomyces cerevisiae and Anabaena spp. A conserved PGCYPT domain...

... all the AGPR sequences suggests that this may be the active center of the protein. Transformation of S. clavuligerus 328, an argC auxotroph deficient in **clavulanic** acid **biosynthesis** , with□plasmid□pULML30, carrying the cloned argC gene, restored both prototrophy and antibiotic **production** .
Descriptors: Aldehyde Oxidoreductases--genetics--GE; *Anti-Bacterial Agents--biosynthesis--BI; * **Clavulanic** Acids-- **biosynthesis** --BI; *Streptomyces--genetics--GE

13/3,K/7 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0011653448 BIOSIS NO.: 199800447695

Construction of genomic library from Streptomyces cattleya A520
AUTHOR: Xiang Longkuan; Wang Yiguang; Dai Jianlu
AUTHOR ADDRESS: Inst. Med. Biotechnol., Chinese Acad. Med. Sci., Peking Union Med. Coll., Beijing 100050, China**China
JOURNAL: Zhongguo Kangshengsu Zazhi 23 (3): p161-165, 237 1998 1998
MEDIUM: print
ISSN: 1001-8689
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: Chinese

ABSTRACT: The genomic library from the S. cattleya A520 was established in E. coli DH1 by using pKC505, a E. coli/ **Streptomyces** cosmid **vector** , in vitro packaging. Foreign DNA fragments and the frequency of insertion in recombinated **plasmid** were 23-30kb in size and over 95% respectively. Assuming that the **Streptomyces** genome is about 104 kb in size, the probability of finding a specific gene from the library composed of 4000 colones is approx 99%. A...

...upstream DNA fragment of the thienamycin cyclase gene isolated from the S. cattleya A520, an IPNS gene from the S. lipmanii and a cs2, a **clavulanic** acid cyclase gene, from the S. clavuligerus were used as probes; 32, 1 and 1 positive clones were isolated from the library, respectively. This result...

...library from the S. cattleya A520 was complete. The relationship among three kinds of clones isolated by different probes and the genes related to thienamycin **biosynthesis** are being studied further.
DESCRIPTORS:
...ORGANISMS: expression **vector** ;

13/3,K/8 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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0009717052 BIOSIS NO.: 199598184885
Expression and purification of two isozymes of clavaminate synthase and initial characterization of the iron binding site
AUTHOR: Busby Robert W; Chang Margaret D-T; Busby Robert C; Wimp Jet; Townsend Craidg A (Reprint)
AUTHOR ADDRESS: Dep. Chem., Johns Hopkins Univ., Baltimore, MD 21218, USA** USA
JOURNAL: Journal of Biological Chemistry 270 (9): p4262-4269 1995 1995
ISSN: 0021-9258
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Clavaminate synthase is an Fe-2+-, O-2-, and alpha-ketoglutarate-dependent oxygenase that catalyzes three transformations in the **biosynthesis** of the important beta-lactamase inhibitor **clavulanic** acid. The genes from **Streptomyces** clavuligerus encoding two isoenzymes of clavaminate synthase have been over-expressed in Escherichia coli to give soluble proteins whose reactions, kinetic properties, and molecular masses...
...presence of histidine and cysteine, respectively, at or near the active site and possibly involved in iron binding. In the course of constructing the expression **vector** , a simply applied general error analysis of the polymerase chain reaction was formulated to calculate the proportion of correctly replicated DNA and guide the design...

13/3,K/9 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0008382418 BIOSIS NO.: 199294084259
CHARACTERIZATION OF THE STREPTOMYCES **-CLAVULIGERUS ARGC GENE ENCODING N ACETYLGLUTAMYLPHOSPHATE REDUCTASE EXPRESSION IN** STREPTOMYCES **-LIVIDANS AND EFFECT ON** CLAVULANIC **ACID** PRODUCTION
AUTHOR: LUDOVICE M (Reprint); MARTIN J F; CARRACHAS P; LIRAS P
AUTHOR ADDRESS: AREA MICROBIOLOGY, FACULTY BIOLOGY, UNIV LEON, 24071 LEON, SPAIN**SPAIN
JOURNAL: Journal of Bacteriology 174 (14): p4606-4613 1992
ISSN: 0021-9193
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

CHARACTERIZATION OF THE STREPTOMYCES **-CLAVULIGERUS ARGC GENE ENCODING N ACETYLGLUTAMYLPHOSPHATE REDUCTASE EXPRESSION IN** STREPTOMYCES **-LIVIDANS AND EFFECT ON** CLAVULANIC **ACID** PRODUCTION

ABSTRACT: The argC gene of **Streptomyces** clavuligerus encoding N-acetylglutamyl-phosphate reductase (AGPR) has been cloned by complementation of argC mutants **Streptomyces** lividans 1674 and Escherichia coli XC33. The gene is contained in an open reading frame of 1,023 nucleotides which encodes a protein of 340...

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13/3,K/10 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE

11619538 EMBASE No: 2002191680
The clavulanic **acid biosynthetic cluster of** Streptomyces **clavuligerus: Genetic organization of the region upstream of the car gene**
Mellado E.; Lorenzana L.M.; Rodriguez-Saiz M.; Diez B.; Liras P.; Barredo J.L.
J.L. Barredo, Area de Biotecnologia, Antibioticos SA, Avenida de Antibioticos 59-61, 24009 Leon Spain
AUTHOR EMAIL: jbarredo@antibioticos.it
Microbiology (MICROBIOLOGY) (United Kingdom) 2002, 148/5 (1427-1438)
CODEN: MROBE ISSN: 1350-0872
DOCUMENT TYPE: Journal ; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 43

The clavulanic **acid biosynthetic cluster of** Streptomyces **clavuligerus: Genetic organization of the region upstream of the car gene**

The genetic organization of the region upstream of the car gene of the **clavulanic** acid biosynthetic gene cluster of **Streptomyces** clavuligerus has been determined. Sequence analysis of a 12.1 kb region revealed the presence of 10 ORFs whose putative functions, according to database searches...

...17-18. Potential transcriptional terminators were identified downstream of ORF11 (fd) and ORF15. Targeted disruption of ORF10 (cyp) gave rise to transformants unable to produce **clavulanic** acid, but with a considerably higher **production** of cephamycin C. Transformants inactivated at ORF14 had a remarkably lower **production** of **clavulanic** acid and similar **production** of cephamycin C. Significant improvements of **clavulanic** acid **production** , associated with a drop in cephamycin C **biosynthesis** , were obtained with transformants of S. clavuligerus harbouring multiple copies of plasmids carrying different constructions from the ORF10-14 region. This information can be used to guide strain improvement programs, blending random mutagenesis and molecular cloning, to optimize the yield of **clavulanic** acid.
MEDICAL DESCRIPTORS:
antibiotic biosynthesis; gene cluster; genetic organization; sequence analysis; open reading frame; gene function; genetic transcription; gene targeting; gene disruption; **plasmid** ; mutagenesis; molecular cloning; nonhuman; controlled study; article; nucleotide sequence; priority journal

13/3,K/11 (Item 2 from file: 73)
DIALOG(R)File 73:EMBASE

07348693 EMBASE No: 1998241612
Construction of genomic library from Streptomyces cattleya A520
Longkuan X.; Yiguang W.; Jianlu D.
X. Longkuan, Institute of Medicinal Biotechnology, Chinese Academy of Medical Sciences, Peking Union Medical College, Beijing 100050 China
Chinese Journal of Antibiotics (CHIN. J. ANTIBIOT.) (China) 1998, 23/3 (161-165)
CODEN: KANGD ISSN: 1001-8689
DOCUMENT TYPE: Journal; Article
LANGUAGE: CHINESE SUMMARY LANGUAGE: ENGLISH; CHINESE
NUMBER OF REFERENCES: 14

The genomic library from the S. cattleya A520 was established in E. coli DH1 by using pKC505, a E. coli/ **Streptomyces** cosmid **vector** , in vitro packaging. Foreign DNA fragments and the frequency of insertion in recombinated **plasmid** were 23~30kb in size and over 95% respectively. Assuming that the **Streptomyces** genome is about 10sup 4 kb in size, the probability of finding a specific gene from the library composed of 4000 colones is approx 99...

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...library from the S. cattleya A520 was complete. The relationship among three kinds of clones isolated by different probes and the genes related to thienamycin **biosynthesis** are being studied further.
?

Set	Items	Description
S1	0	ORF2 (S) (CLAVULANIC)
S2	214	ORF2 (S) (STREPTOMYCES)
S3	0	S2 AND (CLAVULANIC (W) ACID)
S4	274	(CLAVULANIC) (S) (STREPTOMYCES)
S5	0	S4 AND ORF2
S6	0	S2 AND S4
S7	81	S2 AND (GENE (W) (CLUSTER OR CLONING))
S8	35	RD (unique items)
S9	25	S8 NOT PY>1999
S10	851	CLAVULANIC (S) (BIOSYNTHESIS OR PRODUCTION)

```
S11        217   S10 AND S4
S12         20   S11 AND (PLASMID OR VECTOR)
S13         11   RD (unique items)
?
COST
       20oct04 11:53:58 User259876 Session D680.2
            $2.54    0.793 DialUnits File155
               $5.04  24 Type(s) in Format  3
            $5.04  24 Types
     $7.58  Estimated cost File155
            $5.29    0.945 DialUnits File5
              $10.50  6 Type(s) in Format  3
           $10.50  6 Types
    $15.79  Estimated cost File5
            $7.67    0.783 DialUnits File73
              $16.20  6 Type(s) in Format  3
           $16.20  6 Types
    $23.87  Estimated cost File73
            OneSearch, 3 files,  2.521 DialUnits FileOS
     $3.00  INTERNET
    $50.24  Estimated cost this search
    $51.06  Estimated total session cost   2.729 DialUnits
?
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